

REMARKS

Status of the claims

Claims 74-84 and 87-107 were pending in the application. Claims 74-84 and 107 stand rejected, and Claims 87-106 stand objected to under 37 C.F.R. 1.75(c). In accordance with the foregoing, Claims 75, 76, 78, 80, 83, and 87-106 have been amended, Claims 74, 77, 79, 81, 84, and 107 have been newly canceled and Claims 108-111 are newly presented. Specifically, independent Claim 75 had been amended to be directed to a method of treating a cancer disorder selected from the group consisting of melanoma, lung cancer, pancreatic cancer, thyroid cancer, bladder cancer, colon cancer, liver cancer, myeloid leukemia, and villous colon adenoma. Support for this amendment is at page 2, lines 25-29; page 3, lines 9-16; page 6, lines 1-3; and page 20, lines 24-27, the art of record and elsewhere in the application as filed. No new matter is presented.

Claim objections

Claims 87-106 stand objected to under 37 C.F.R. 1.75(c) as being in improper form, and have not been examined on their merits. In view of the foregoing amendments to Claims 87, 88, 90, 91, 93, 94, 96, 99-101 and 104-106, which now recite "A method of any one of claim 75, 76, 78, 80, 82, or 83," or similar language, this objection is now moot. Reconsideration and examination of these claims on their merits is requested.

Rejection of Claims 75-84 and 107 under 35 U.S.C. § 112

Claims 75-84 and 107 stand rejected under 35 U.S.C. § 112, first paragraph, on the basis that the specification does not reasonably provide enablement for treating any cancer disorder in general mediated by Ras mitogen-activated protein kinase pathway. The Examiner did note, however, that the specification was enabling for treating some particular/specific cancer disorders in a human or animal comprising administering a composition comprising compounds

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represented by formula (I). The Examiner asserted that the specification does not enable any person skilled in the art "to practice the invention commensurate in scope with the claims."

Without acquiescing in the Examiner's assertions, and in order to facilitate prosecution of the claims in the application, independent Claim 75 has been amended to limit its scope to specific clearly enabled cancer disorders. Specifically, Claim 75 was amended to incorporate the limitations of Claim 107 (now canceled), which recite several Ras/mitogen-activated protein kinase signal pathway-mediated cancer disorders, including melanoma, lung cancer, pancreatic cancer, thyroid cancer, bladder cancer, colon cancer, liver cancer, myeloid leukemia, and villous colon adenoma. Further, Claim 78 has been amended to include the limitations of Claim 79 (now canceled), wherein the hormone dependent cancer disorder is breast cancer or prostate cancer. Claim 82, which is already limited to hematological cancer disorders, has not amended.

In addition to the information presented in applicants' prior submissions, additional support for the strong correlation between Ras/mitogen-activated protein kinase signal pathway-mediated disorders, particularly cancer, and the role of Ras, Raf, and related kinases and kinase substrates in modulating the balance of growth factors and metabolites controlling cell division and death, can be found in Rowinsky, E.K., et al., "Ras Protein Farnesyltransferase: A Strategic Target for Anticancer Therapeutic Development," *Journal of Clinical Oncology* 17(11):3631-3652, 1999, a copy of which is submitted herewith as Exhibit A. While Rowinsky et al. is primarily directed to reviewing progress in the development of farnesyltransferase inhibitors, it does provide a summary of literature relating to tumor types that harbor *ras* mutations. Table 1 on page 3635, for example, notes the frequency of *ras* mutations and the predominant *ras* mutation in the following types of tumors/cancer: acute myelogenous leukemia, bladder, breast, myelodysplastic syndrome, cervix, cholangiocarcinoma, colon (adenocarcinoma and adenoma), embryonal rhabdomyosarcomas, endometrial carcinoma, liver, lung (large-cell carcinoma and

adenocarcinoma), kidney, melanoma, multiple myelomas, oral squamous cell carcinoma, ovarian carcinoma, pancreatic carcinoma, seminoma, skin (keratoacanthoma), thyroid (follicular adenoma, follicular carcinoma, papillary carcinoma, and undifferentiated carcinoma).

In view of the amendments presented herein and applicants' previously submitted arguments and references, the Examiner's rejection of Claims 75-84 and 107 under 35 U.S.C. § 112, first paragraph, is believed to be overcome. Reconsideration and withdrawal of this rejection is requested.

Rejection of Claims 76, 78 and 83 under 35 U.S.C. § 112

Claims 76, 80, and 83 stand rejected under 35 U.S.C. § 112, first paragraph, on the basis that while being enabled for a specific agent selected from irinotecan, topotecan, gemcitabine, 5-fluorouracil, leucovorin, carboplatin, cisplatin, taxanes, tezacitabine, cyclophosphamide, imatinib, specific anthrocyclines, rituximab, trastuzumab for the treatment of specific cancer disorders mediated by Ras mitogen-activated protein kinase pathway, the application does not reasonably provide enablement for a method of treating cancer in a human or animal subject comprising administering a compound represented by Formula (I) and agents in general.

As set forth above, Claims 76, 80, and 83 have been amended to recite specific additional agents for the treatment of cancer, and this rejection is now moot.

Rejection of Claim 74 under 35 U.S.C. § 112

Claim 74 stands rejected under 35 U.S.C. § 112, first paragraph, on the basis that the specification does not reasonably provide enablement for treating any disorder mediated by Raf kinase activity. Without acquiescence in the Examiner's rejection and solely for the purposes of reducing outstanding issues in the present application, Claim 74 has been cancelled without prejudice to applicants' right to pursue claims to this subject matter in a separate application. This rejection is now moot.

New Claims 108-111


New Claims 108-111 depend from and further limit Claim 75 to recite various specific embodiments of the invention. In accordance with the comments above, these claims are also believed to be in condition for allowance.

CONCLUSION

Entry of the foregoing amendments, reconsideration and prompt favorable action are requested. The Examiner is requested to contact the applicants' representative at the number set forth below to discuss any issues that will facilitate prosecution of the application.

Respectfully submitted,

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A handwritten signature in black ink, appearing to read "Dennis K. Shelton", is written over the printed name.

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